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SYSTEMIC LUPUS ERYTHEMATOSUS WITH DEFICIENCY OF THE T4 EPITOPE ON T4 HELPER/INDUCER CELLS

To the Editor: Stohl et al. (June 27 issue) contend that the altered T4 phenotype in their three patients with systemic lupus erythematosus (SLE) accounted for the impaired helper/inducer-cell function of blood lymphocytes in vitro.[1] However, they present no formal evidence to support this claim. Peripheral-blood mononuclear cells from the three probands were clearly deficient in their capacity to generate immunoglobulin-secreting cells when stimulated with the polyclonal B-cell activator pokeweed mitogen. As previously reported,[2] this finding is a general characteristic of cells from patients with SLE who have phenotypes with the T4 epitope intact. Therefore, the authors focused on the five first-degree relatives from the three families who had the altered phenotype. One of these subjects had a response well within the normal range. Of the other four, whose responses were reduced, one had lymphadenopathy and another had positive serologic findings (antinuclear antibody, anti-extractable nuclear antigen, and rheumatoid factor). This sample size is far too small to draw any conclusions about the relation of altered T4 phenotype and impaired helper/inducer function. More important, the authors have not excluded several other possible explanations for impaired pokeweed mitogen–induced B-cell differentiation, including reduced numbers or impaired function of B cells or monocytes, or excessive suppressor T-cell activity. The authors also erroneously interpreted a report by Rogozinski et al.[3] In vitro studies carried out by the latter group indicated that the T4 epitope detected by the OKT4 monoclonal antibody was not critical to inducing helper function of B-cell differentiation. Instead, the studies highlighted the importance of other epitopes on the T4 molecule. This point is in accord with the observation that ostensibly healthy persons have the T4 epitope–deficient phenotype, as well as with findings recently reported by our group in a patient with this phenotypic abnormality.[4]

A 56-year-old black man had red-cell aplasia, thymoma, and hypogammaglobulinemia, without evidence of SLE or lymphadenopathy. He also had impaired pokeweed mitogen–induced B-cell differentiation, which was explained in part by the absence of B cells from his peripheral blood. In addition, his T cells (OKT8 phenotype) demonstrated augmented suppression of pokeweed mitogen–induced B-cell differentiation. Furthermore, when suppressor activity was abrogated, the patient's T4 cells were capable of providing help for pokeweed mitogen–induced B-cell differentiation. Our data suggest that the T4-deficient, Leu-3A–positive T cell subserves helper/inducer activity normally in vitro and in vivo (intact delayed hypersensitivity), and that the deficiency of the T4 epitope on T helper/inducer cells does not alter the ability of these cells to provide T-cell help. Since our patient's clinical disorders as well as SLE were associated with immunoregulatory and autoimmune disturbances, it is possible that the T4 epitope–deficient phenotype predisposes to a wide range of immunoregulatory abnormalities.

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To the Editor: In their report on three black Jamaicans with SLE whose T helper/inducer cells lacked the T4 epitope, Stohl et al. noted that heterogeneity in expression of the T4 epitope has never been reported in whites. We wish to describe a white subject whose cells exhibited the heterozygous T4 epitope phenotype.

As part of a large population-based survey of healthy subjects in the Washington (D.C.) metropolitan area, peripheral-blood mononuclear cells from 392 randomly selected persons 20 to 69 years old (297 whites and 95 blacks) were studied by flow microfluorometry using a panel of monoclonal antibodies, including OKT4 and OKT4A (Ortho Diagnostics, Raritan, N.J.). Seven of the 95 black subjects (7.4 per cent) had no detectable OKT4+ cells (T4 epitope–deficient phenotype). They did have normal percentages and fluorescence intensity characteristic of OKT4A+, OKT3+, and OKT8+ cells. In addition, 26 blacks (27.4 per cent) had normal numbers of OKT4A cells but a 50 per cent reduction in fluorescence intensity of OKT4 cells as compared with OKT4A cells, giving an estimated gene frequency of the T4 epitope–deficiency allele in blacks of 0.21. The other blacks (65.2 per cent) had full expression of the T4 epitope. Cells from one white subject, a healthy 36-year-old man, exhibited a 50 per cent reduction in mean fluorescence intensity of OKT4 as compared with OKT4A when tested on two occasions.

Recent reports have presented strong evidence that T4 epitope expression is inherited as a mendelian codominant trait.[1,2] The distribution of T4 phenotypes among our black subjects fits the Hardy–Weinberg equilibrium, further supporting a mendelian pattern of inheritance. Studies of blacks from other areas of the United States,[1,2] the Caribbean,[3] and South Africa[3] have revealed similar distributions of T4 polymorphism. Amino et al.[4] found that 38 of 8866 consecutive samples (0.43 per cent) tested at a large laboratory in Japan had no T4 expression. Although presumably the subjects were Japanese, no data on race or ethnic background were provided. Another study identified three members of a Japanese family whose lymphocytes did not express the T4 epitope,[5] thus demonstrating the presence of T4 heterogeneity in the Japanese population. It is possible that our subject may have had some black or Japanese ancestry of which he was unaware. Further population studies using OKT4 together with a monoclonal antibody against another epitope of the T4 antigen (i.e., Leu-3 [Becton Dickinson, Mountain View, Calif.] or OKT4A) may help to clarify the racial and ethnic diversity of T4 epitope expression.

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To the Editor: Stohl et al. described several Jamaican patients with SLE who had OKT4 epitope–deficient (OKT4−) helper T lymphocytes. These results led the authors to suggest an association between absence of the OKT4 epitope and SLE. The OKT4−,